

General

Guideline Title

British Association of Dermatologists' guidelines for the management of bullous pemphigoid 2012.

Bibliographic Source(s)

Venning VA, Taghipour K, Mohd Mustapa MF, Highet AS, Kirtschig G. British Association of Dermatologists' guidelines for the management of bullous pemphigoid 2012. Br J Dermatol. 2012 Dec;167(6):1200-14. [116 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Wojnarowska F, Kirtschig G, Highet AS, Venning VA, Khumalo NP. Guidelines for the management of bullous pemphigoid. Br J Dermatol 2002 Aug;147(2):214-21. [48 references]

Recommendations

Major Recommendations

Definitions for the levels of evidence (1++, 1+, 1-, 2++, 2+, 2-, 3, 4) and strength of recommendations (A-D) are presented at the end of the "Major Recommendations" field.

Diagnosis

Laboratory Diagnosis of Bullous Pemphigoid (BP)

A skin biopsy from a fresh blister stained with haematoxylin and eosin shows subepidermal cleaving and an inflammatory infiltrate mainly consisting of eosinophils; however, the diagnosis is confirmed with immunofluorescence studies (IF). A biopsy for direct IF (DIF) is taken from uninvolved skin about 1 cm away from a fresh blister and is immediately snap-frozen in liquid nitrogen or transported in either Michel's transport medium or normal (0.9%) saline. If using saline, the biopsy must be processed within 24–48 h; with Michel's medium prompt handling is to be preferred, but a longer delay of up to 2 weeks may still yield results. Indirect IF (IIF) is performed on serum, and if this is not obtainable, on blister fluid. The characteristic DIF picture in BP is a linear deposition of immunoglobulin G (IgG) and/or complement component 3 (C3) along the basement membrane zone (BMZ). Other immunoglobulins, including immunoglobulin A (IgA), immunoglobulin M (IgM) and immunoglobulin E (IgE), may also be present. Substrates used for IIF include monkey oesophagus and normal human skin; the latter can be split using molar saline. Antibodies in BP serum usually detect antigens at the roof of the salt-split skin. In most cases this may help to differentiate BP from other immunobullous diseases such as epidermolysis bullosa acquisita (EBA) and some cases of mucous membrane pemphigoid (MMP), in both of which antibodies are deposited on the dermal aspect of the split skin.

Over recent years, enzyme-linked immunosorbent assay (ELISA) has emerged as an additional diagnostic technique for some autoimmune bullous

diseases. Serum levels of antibodies to both BP180 and BP230 can be measured with commercially available ELISA kits, with the BP180 ELISA being more sensitive than the BP230 ELISA. The NC16A domain is an important pathogenic epitope of the BP180 antigen and is used in BP180 ELISA to detect antibody titres that reportedly correlate with disease activity. In one study, false-positive ELISA results using the same commercial kits were reported in 7.4% of sera with negative IIF. The ELISA is currently not widely available in the United Kingdom but is a useful additional diagnostic tool in selected cases and in research. IF studies remain the gold standard for diagnosis.

Differential Diagnosis

Autoimmune bullous diseases may overlap in morphology and immunopathology; however, factors such as age of onset, course of the disease, absence of scarring and extent of mucosal involvement are important in differentiating the diagnosis. DIF and salt-split IIF are useful in distinguishing BP from other subepidermal diseases, namely linear IgA disease, MMP and EBA.

Blisters occur in genetic bullous diseases, in particular the epidermolysis bullosa group and may also be caused by insect bites, burns, oedema, cellulitis, erythema multiforme, and contact dermatitis. Viral and bacterial skin infections should be recognized and treated before treatment with immunosuppressant therapy is initiated.

Management

BP is usually a self-limiting disease with a clinical course that may last from months to years. During the active stage, the disease is associated with significant morbidity and a mortality twice that of the general elderly population. Older age at onset and frail general condition are poor prognostic factors. Many available treatments are associated with toxicity and may be poorly tolerated in patients with BP. Mortality during the first year is significantly higher in patients treated with high doses of systemic corticosteroids (prednisolone equivalent >40 mg daily). Treatment should aim to control symptoms with minimum adverse effects where possible. Options are broadly divided into anti-inflammatory drugs, immunosuppressive or immunomodulating drugs, and procedures aiming to remove circulating pathogenic antibodies and inflammatory mediators. The choice of treatment depends on the individual patient's circumstances especially the severity of the BP and the presence of comorbidities.

Systemic Steroids (Strength of Recommendation A; Level of Evidence 1+)

Systemic corticosteroid therapy was demonstrated to be effective in BP in uncontrolled clinical studies during the 1950s and has become established as the mainstay of treatment. The effect in most cases is rapid, with suppression of inflammation and blistering typically achieved within 1–4 weeks, after which the dose is gradually reduced. The most commonly used drugs are prednisone and prednisolone which are assumed to be bioequivalent.

General conclusions from the studies are:

1. Systemic steroids are the best established treatment for BP.
2. Immunosuppressive and metabolic adverse effects occur and are dose-dependent.
3. Doses of prednisolone of 0.75–1.0 mg/kg daily in widespread BP are effective within 1–4 weeks in about 60–90% of cases.

Clinical experience suggests that the more severe the disease, the larger the dose of steroid is required (up to 1 mg/kg daily), although this has not been rigorously proven. A minority of patients with BP respond poorly to such doses of systemic steroid; increasing the dose confers little additional benefit and is significantly more toxic.

It is not possible to identify a starting dose of prednisolone (or prednisone) that would be maximally effective and minimally toxic for all patients with BP. Doses which might meet these criteria for a majority of patients are:

1. 0.75 mg/kg for patients with severe involvement
2. 0.5 mg/kg for moderate disease
3. 0.3 mg/kg for mild or localized disease

If new inflammatory or blistered lesions are few or absent within 4 weeks, the treatment can be regarded as successful and the dose of steroid should then be gradually reduced. A reduction of the daily dose of prednisolone at fortnightly intervals, initially by about one-third or one-quarter down to 15 mg daily, then by 2.5 mg decrements down to 10 mg daily, is suggested. The dose could then be reduced by 1 mg each month. In about 50% of cases relapse will occur at some point during the dose-reduction period, indicating that the previous dose is likely to be the minimal effective dose for that patient.

For patients with widespread BP who do not respond to these doses, or who relapse on unacceptably high doses, other agents, alone or in addition to the systemic steroid, may be preferable to higher doses of steroid.

The duration of systemic steroid treatment in BP is likely to be many months and is sometimes indefinite. Gastric protection, usually with a proton

pump inhibitor, should be considered. Measures aimed at minimizing loss of bone density are appropriate in postmenopausal women and men over 50 years, and in any patient at increased risk of fragility fracture, who are expected to take prednisolone 7.5 mg or more daily for at least 3 months. Patients with BP (and also patients with pemphigus vulgaris) were reported to have lower levels of vitamin D, and a higher incidence of severe hypovitaminosis D, than controls, suggesting additional risk of bone density loss. Calcium and vitamin D supplementation and a bisphosphonate are usually recommended and have been shown to be effective in preserving bone density, if given from the start of systemic steroid therapy in patients with immunobullous diseases. Calcium may impair absorption of mycophenolate mofetil (MMF) and oral bisphosphonates and should be taken at a different time.

Topical Corticosteroids (Strength of Recommendation A; Level of Evidence 1+)

Very potent topical steroids (clobetasol propionate) are an effective treatment for BP and they seem to have less serious adverse effects compared with 1 mg/kg of prednisone per day. However, their use in extensive disease may be limited by practical factors (e.g. ability of patient or availability of carer to apply the treatment) and they may be associated with systemic absorption and adverse events. When feasible they should be considered for first-line treatment, especially in localized disease.

Azathioprine (Strength of Recommendation D; Level of Evidence 4)

After systemic steroids, azathioprine is still a commonly used drug in BP. It is mostly employed in doses of up to 2.5 mg/kg daily as an adjunct to systemic steroids for its presumptive steroid-sparing effect.

Azathioprine dose can be optimized with regard to myelosuppression risk by prior assay of thiopurine methyltransferase (TPMT) activity, a test that is now widely available in the United Kingdom (U.K.) and relatively inexpensive. However, a normal TPMT level does not totally preclude myelotoxicity and regular monitoring of blood counts and liver function are essential.

There is currently insufficient evidence of benefit to recommend routine addition of azathioprine to systemic steroids for the control of BP. In view of its side-effect profile, it is recommended that azathioprine only be considered as an adjunctive treatment to prednisolone where response has been inadequate and the disease is not suppressed, or where the side-effects of existing therapy are troublesome and unacceptable.

Anti-inflammatory Antibiotics and Nicotinamide (Strength of Recommendation D; Level of Evidence 4)

Erythromycin should be considered for treatment, particularly in children (adult dose 1000–3000 mg daily), and perhaps in combination with topical corticosteroids. A beneficial effect may be seen within 1–3 weeks of commencing treatment.

Tetracyclines and nicotinamide may be considered as treatment in adults, perhaps in combination with topical corticosteroids. However, apart from one case report of niacinamide (nicotinamide) as monotherapy in localized BP, there is no evidence for its effectiveness as a sole treatment of BP. The optimum doses, both for the antibiotics and nicotinamide, are not established. Nicotinamide is used between 500 and 2500 mg daily, usually started at 500 mg daily and then gradually increased to 1500–2500 mg daily to minimize gastric side effects. Tetracycline has been used at doses of 500–2000 mg daily, doxycycline at 200–300 mg daily and minocycline at 100–200 mg daily. Tetracycline should be avoided in renal impairment as should doxycycline and minocycline in patients with hepatic impairment. Minocycline has a worse side-effect profile and is therefore not the first choice of antibiotic. A few cases of minocycline-associated pneumonia and eosinophilia have been described, necessitating immediate withdrawal. Lymecycline has a beneficial side-effect profile and has been successfully used by some dermatologists (408 mg twice daily) in the U.K. without published evidence. When blister formation is suppressed sufficiently the antibiotics and nicotinamide must be reduced slowly, one at a time, over several months to avoid relapse.

Methotrexate (MTX) (Strength of Recommendation D; Level of Evidence 4)

The most important toxicities of MTX are myelosuppression, hepatotoxicity, and pneumonitis. MTX is excreted renally, which should be considered in the elderly and may explain the low doses required for disease control. Many investigators recommend folic acid 5 mg on the non-MTX days to reduce some adverse effects, but this is not proven.

Evidence from case series suggests that MTX can be effective at controlling BP, either as a monotherapy or in combination with topical or systemic steroids.

Dapsone and Sulfonamides (Strength of Recommendation D; Level of Evidence 3)

Glucose-6-phosphate dehydrogenase deficiency predisposes to haematological side-effects and should be excluded in predisposed races (e.g. those of African, Middle Eastern, and South Asian origin), and all patients receiving dapsone need very frequent monitoring of blood count and liver function in the early months. The side-effect profile of dapsone and sulfonamides is potentially hazardous in the elderly. In this age group, these treatments should be considered only if other treatments are ineffective or contraindicated, and treatment started at low doses (50 mg daily) to be

increased by 50 mg daily in 2-weekly steps to a maximum of 150–200 mg daily.

Intravenous Immunoglobulins (Strength of Recommendation D; Level of Evidence 3)

Intravenous immunoglobulin (IVIg) is well tolerated but expensive, costing £5320.00 per cycle of 2 g/kg in a 70-kg patient. U.K. guidance on its use is available from the Department of Health (<http://www.dh.gov.uk>). IVIg should only be considered as an adjunctive treatment in patients with very severe disease where rapid control is needed, or when there is failure with or contraindication to other treatments.

Chlorambucil (Strength of Recommendation D; Level of Evidence 3)

Chlorambucil as an adjunct to systemic steroids should be considered as an alternative to other more established immunosuppressants if these have failed or are poorly tolerated or contraindicated. Careful monitoring is required for possible haematological toxicity.

Cyclophosphamide

Cyclophosphamide is more toxic than other immunosuppressive drugs used for BP. It may rarely be considered for exceptionally refractory disease.

Ciclosporin

Ciclosporin cannot be recommended in the routine treatment of BP. It may rarely have a place in refractory cases but its value is likely to be limited by renal toxicity, especially in the elderly.

Other Treatments

Topical Tacrolimus (Strength of Recommendation D; Level of Evidence 3)

Individual case reports have described a response to topical treatment with the calcineurin inhibitor, tacrolimus. It has mainly been used for localized and limited generalized disease. The use of topical tacrolimus is limited by local irritation and its price compared with topical steroids. It may be useful as an alternative in localized and limited disease without the disadvantage of causing skin atrophy.

Biologic Agents

- Rituximab (Strength of Recommendation D; Level of Evidence 3)
- Antitumour necrosis factor- α agents (Strength of Recommendation D; Level of Evidence 3)
- Other biologic agents (Strength of Recommendation D; Level of Evidence 3)

Biological drugs are expensive and may be associated with potentially serious adverse effects; until further supportive evidence is available, their role in BP remains limited.

Plasmapheresis and Immunoapheresis (Strength of Recommendation D; Level of Evidence 3)

Plasmapheresis and immunoapheresis have no role in the routine treatment of BP, although in cases of refractory BP or when reduction of immunosuppressive drugs is necessary due to intolerance and adverse effects, these modalities may be used as adjuvant treatment.

Childhood Bullous Pemphigoid (Strength of Recommendation D; Level of Evidence 3)

Although there is no evidence to support any particular treatment strategy in childhood and infantile BP, its generally short-lived and benign nature suggests that preference should be given to low-toxicity treatments such as erythromycin and topical steroids.

Skin Care in Bullous Pemphigoid (Strength of Recommendation D; Good Practice Point)

There are no studies on this topic and the following recommendations are based on the personal experience of the authors. Blisters should generally be left intact if possible as this may help prevent secondary bacterial infection. When they are particularly large or in sites where they are troublesome or interfere with function, such as the sole of the foot, blisters may be pierced with a sterile needle releasing the fluid, but leaving the blister roof in place. If there are extensive areas of erosion and open raw areas, antiseptics such as potassium permanganate as a bath or soaks, or antiseptic-containing bath oils (e.g. Dermol 600® [Dermal Laboratories, Hitchin, U.K.] or Oilatum Plus® [Steifell Laboratories, High Wycombe, U.K.]) may be used for a few days to dry the lesions and prevent infection. Painful eroded or raw areas may be covered with a low-adhesion dressing such as Mepitel® (Mölnlycke, Dunstable, U.K.) or Atrauman® (Hartmann, Heywood, U.K.) held in place with soft elasticated viscous stockinette (e.g. Comifast® [Synergy, Swindon, U.K.], Tubifast® [Mölnlycke]). It is important to ensure that such areas of erosion are included in treatment with topical steroids (clobetasol propionate).

Follow-up

BP is frequently a chronic disease and ideally patients should be followed until they are in complete remission and off all treatment. Patients should be monitored for drug side-effects and to ensure that symptoms are controlled to their satisfaction without excessive doses of topical or systemic treatment. Occasional itching or lesions (if acceptable to the patient) indicates that they are not being overtreated. Once their disease is stable, an attempt should be made to wean treatment at roughly 2–4 weekly intervals; this should be done on clinical criteria rather than by IF testing.

Definitions:

Levels of Evidence

| Level of Evidence | Type of Evidence |
|-------------------|---|
| 1++ | High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias |
| 1+ | Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias |
| 1- | Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias* |
| 2++ | High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal |
| 2+ | Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal |
| 2- | Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal* |
| 3 | Nonanalytical studies (for example, case reports, case series) |
| 4 | Expert opinion, formal consensus |

*Studies with a level of evidence '1-' should not be used as a basis for making a recommendation.

Strength of Recommendations

| Class | Evidence |
|---------|---|
| A | <ul style="list-style-type: none">At least one meta-analysis, systematic review, or randomized controlled trial (RCT) rated as 1++, and directly applicable to the target population, orA systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of resultsEvidence drawn from a National Institute for Health and Clinical Excellence (NICE) technology appraisal |
| B | <ul style="list-style-type: none">A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results, orExtrapolated evidence from studies rated as 1++ or 1+ |
| C | <ul style="list-style-type: none">A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, orExtrapolated evidence from studies rated as 2++ |
| D | <ul style="list-style-type: none">Evidence level 3 or 4, orExtrapolated evidence from studies rated as 2+, or Formal consensus |
| D (GPP) | <ul style="list-style-type: none">A good practice point (GPP) is a recommendation for best practice based on the experience of the guideline development group. |

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Bullous pemphigoid (BP)

Guideline Category

Diagnosis

Management

Treatment

Clinical Specialty

Dermatology

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide up-to-date, evidence-based recommendations for the management of bullous pemphigoid (BP)
- To update and expand on the previous guidelines by: (i) offering an appraisal of all relevant literature since January 2002, focusing on any key developments; (ii) addressing important, practical clinical questions relating to the primary guideline objective; (iii) providing guideline recommendations and, where appropriate, with some health economic implications discussing potential developments and future directions

Target Population

Patients with known or suspected bullous pemphigoid (BP)

Interventions and Practices Considered

Diagnosis

1. Biopsy
2. Histological examination of tissue
3. Immunopathological examination of tissue (direct) or serum (indirect) immunofluorescence
4. Enzyme-linked immunosorbent assay (ELISA)
5. Differential diagnosis

Treatment

1. Systemic corticosteroids
2. Topical corticosteroids
3. Anti-inflammatory antibiotics and nicotinamide (niacinamide)
4. Azathioprine
5. Methotrexate
6. Dapsone
7. Mycophenolate mofetil
8. Sulphonamides
9. Intravenous immunoglobulins
10. Chlorambucil
11. Cyclophosphamide
12. Cyclosporin
13. Other treatments (not recommended routinely)
 - Topical tacrolimus
 - Biological agents
 - Plasmapheresis and immunoapheresis

Management

1. Skin care
2. Follow-up
3. Monitoring of drug therapy

Major Outcomes Considered

- Sensitivity and false positive rates for diagnostic tests
- Effectiveness of treatments
- Rate of treatment response
- Rate of disease relapse/recurrence
- Adverse effects of treatment, including morbidity and mortality
- Treatment costs

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

PubMed, MEDLINE and EMBASE databases were searched up to June 2012 for meta-analyses, randomized and nonrandomized controlled clinical trials, case series, case reports, and open studies involving bullous pemphigoid, with no language exclusions; search terms and strategies are detailed in Appendix S1 (see the "Availability of Companion Documents" field).

Additional relevant references were also isolated from citations in the reviewed literature, as well as (independent) targeted searches carried out by coauthors. Working in pairs, the authors screened the identified titles, and those relevant for first-round inclusion were selected for further scrutiny. The abstracts for the shortlisted references were then reviewed and the full papers of relevant material were obtained; disagreements in the final

selections were resolved by discussion with the entire development group. Additional selection criteria included relevant publications on the management of childhood bullous pemphigoid (BP).

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

| Level of Evidence | Type of Evidence |
|-------------------|---|
| 1++ | High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias |
| 1+ | Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias |
| 1- | Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias* |
| 2++ | High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal |
| 2+ | Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal |
| 2- | Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal* |
| 3 | Nonanalytical studies (for example, case reports, case series) |
| 4 | Expert opinion, formal consensus |

*Studies with a level of evidence '-' should not be used as a basis for making a recommendation.

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The guideline development group consisted of consultant dermatologists.

This set of guidelines has been developed using the British Association of Dermatologists' recommended methodology (see the "Availability of Companion Documents" field) and with reference to the Appraisal of Guidelines Research and Evaluation (AGREE II) instrument (see the "Availability of Companion Documents" field). Recommendations were developed for implementation in the National Health Service using a process of considered judgment based on the evidence.

Following completion of the literature search, the structure of the 2002 guidelines was discussed and re-evaluated, and different coauthors were allocated separate subsections. Each coauthor then performed a detailed appraisal of the selected literature with discussions with the entire development group to resolve any issues, e.g. with the quality of evidence and making the appropriate recommendations. All subsections were subsequently collated and edited to produce the final guideline.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

| Class | Evidence |
|----------------|---|
| A | <ul style="list-style-type: none">At least one meta-analysis, systematic review, or randomized controlled trial (RCT) rated as 1++, and directly applicable to the target population, orA systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of resultsEvidence drawn from a National Institute for Health and Clinical Excellence (NICE) technology appraisal |
| B | <ul style="list-style-type: none">A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results, orExtrapolated evidence from studies rated as 1++ or 1+ |
| C | <ul style="list-style-type: none">A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, orExtrapolated evidence from studies rated as 2++ |
| D | <ul style="list-style-type: none">Evidence level 3 or 4, orExtrapolated evidence from studies rated as 2+, or Formal consensus |
| D (GPP) | <ul style="list-style-type: none">A good practice point (GPP) is a recommendation for best practice based on the experience of the guideline development group. |

Cost Analysis

Published cost analyses were reviewed:

- Although the treatments were equally effective, the 5.5-fold higher cost of mycophenolate mofetil (MMF) (2 g daily) compared with azathioprine (2 mg/kg daily for a 75-kg patient) could be an important consideration in some health economies.
- Intravenous immunoglobulin (IVIg) is well tolerated but expensive, costing £5320.00 per cycle of 2 g/kg in a 70-kg patient.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline development group consisted of consultant dermatologists. The draft document was circulated to the British Association of

Dermatologists (BAD) membership, the British Dermatological Nursing Group (BDNG), the Primary Care Dermatological Society (PCDS), and the Pemphigus Vulgaris Network for comments, and was peer reviewed by the Clinical Standards Unit of BAD (made up of the Therapy and Guidelines subcommittee) prior to publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of bullous pemphigoid

Potential Harms

- Immunosuppressive and metabolic adverse effects occur with use of systemic steroids and are dose-dependent.
- Gastric protection, usually with a proton pump inhibitor, should be considered when treating with systemic steroids. Measures aimed at minimizing loss of bone density are appropriate in postmenopausal women and men over 50 years, and in any patient at increased risk of fragility fracture, who are expected to take prednisolone 7.5 mg or more daily for at least 3 months. Patients with bullous pemphigoid (BP) (and also patients with pemphigus vulgaris) were reported to have lower levels of vitamin D, and a higher incidence of severe hypovitaminosis D, than controls, suggesting additional risk of bone density loss.
- Adverse effects of topical corticosteroids may include diabetes mellitus, cardiovascular and neurovascular disorders, severe infections, and cutaneous side effects, including purpura, severe skin atrophy, and striae.
- Very potent topical steroids (clobetasol propionate) are an effective treatment for BP and they seem to have less serious adverse effects compared with 1 mg/kg of prednisone per day. However, they may be associated with systemic absorption and adverse events.
- Adverse effects of azathioprine may include hepatotoxicity and myelotoxicity.
- Azathioprine dose can be optimized with regard to myelosuppression risk by prior assay of thiopurine methyltransferase (TPMT) activity, a test that is now widely available in the United Kingdom and relatively inexpensive. However, a normal TPMT level does not totally preclude myelotoxicity and regular monitoring of blood counts and liver function are essential.
- Adverse effects of anti-inflammatory antibiotics and nicotinamide may include gastrointestinal upset, pigmentation, and *Candida* infection.
- The most important toxicities of methotrexate (MTX) are myelosuppression, hepatotoxicity, and pneumonitis. Many investigators recommend folic acid 5 mg on the non-MTX days to reduce some adverse effects, but this is not proven.
- Glucose-6-phosphate dehydrogenase deficiency predisposes to haematological side-effects and all patients receiving dapsone need very frequent monitoring of blood count and liver function in the early months. The side-effect profile of dapsone and sulfonamides is potentially hazardous in the elderly.
- Careful monitoring is required for possible haematological toxicity when treating with chlorambucil.
- Cyclophosphamide is more toxic than other immunosuppressive drugs used for BP.
- Ciclosporin may rarely have a place in refractory cases but its value is likely to be limited by renal toxicity, especially in the elderly.
- The use of topical tacrolimus is limited by local irritation and its price compared with topical steroids.
- Biological drugs are expensive and may be associated with potentially serious adverse effects.

Contraindications

Contraindications

- Glucose-6-phosphate dehydrogenase deficiency predisposes to haematological side-effects and should be excluded in predisposed races (e.g., those of African, Middle Eastern, and South Asian origin).
- Tetracycline should be avoided in renal impairment as should doxycycline and minocycline in patients with hepatic impairment.

Qualifying Statements

Qualifying Statements

This document has been prepared on behalf of the British Association of Dermatologists (BAD) and is based on the best data available when the document was prepared. It is recognized that under certain conditions it may be necessary to deviate from the guidelines and that the results of future studies may require some of the recommendations herein to be changed. Failure to adhere to these guidelines should not necessarily be considered negligent, nor should adherence to these recommendations constitute a defence against a claim of negligence.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Audit Criteria/Indicators

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Venning VA, Taghipour K, Mohd Mustapa MF, Highet AS, Kirtschig G. British Association of Dermatologists' guidelines for the management of bullous pemphigoid 2012. Br J Dermatol. 2012 Dec;167(6):1200-14. [116 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2002 Aug (revised 2012 Dec)

Guideline Developer(s)

British Association of Dermatologists - Medical Specialty Society

Source(s) of Funding

British Association of Dermatologists

Guideline Committee

British Association of Dermatologists Therapy & Guidelines Subcommittee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

None declared

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Wojnarowska F, Kirtschig G, Highet AS, Venning VA, Khumalo NP. Guidelines for the management of bullous pemphigoid. Br J Dermatol 2002 Aug;147(2):214-21. [48 references]

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [British Association of Dermatologists Web site](#)

Availability of Companion Documents

The following are available:

- Bell HK, Ormerod AD. Writing a British Association of Dermatologists clinical guideline: an update on the process and guidance for authors. Br J Dermatol 2009; 160:725-8. Electronic copies: Available in Portable Document Format (PDF) from the [British Association of Dermatologists Web site](#) .

Literature search strategies are available from the [British Journal of Dermatology Web site](#) .

In addition, recommended audit points are provided in section 13 of the [original guideline document](#) .

Patient Resources

The following is available:

- Pemphigoid. Patient information leaflet. London (England): British Association of Dermatologists; 2012 Jan. 4 p. Available in Portable Document Format (PDF) from the [British Association of Dermatologists Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on April 22, 2005. The information was verified by the guideline developer on June 27, 2005. This summary was updated by ECRI Institute on November 6, 2007, following the U.S. Food and Drug Administration advisory on CellCept (mycophenolate mofetil). This NGC summary was updated by ECRI Institute on February 6, 2013. The updated information was verified by the guideline developer on March 6, 2013. This summary was updated by ECRI Institute on November 21, 2013 following the U.S. Food and Drug Administration advisory on Arzerra (ofatumumab) and Rituxan (rituximab).

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